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ANALYSIS, REMOVAL, EFFECTS AND RISK OF PHARMACEUTICALS IN THE WATER CYCLE

OCCURRENCE AND TRANSFORMATION
IN THE ENVIRONMENT

MIRA PETROVIC, SANDRA PÉREZ
AND DAMIA BARCELO

SECOND EDITION

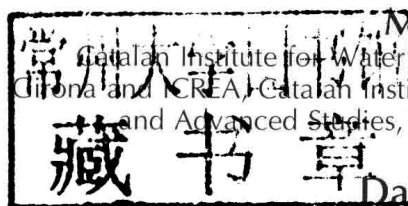
Analysis, Removal, Effects and Risk of Pharmaceuticals in the Water Cycle

Occurrence and Transformation in the
Environment

Comprehensive Analytical Chemistry

Volume 62

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Series Editor's Preface

Sometime in 2007, I wrote that, as series editor of Comprehensive Analytical Chemistry, I have certain duties. The first is to be able to acquire new titles for this successful series in the field of analytical chemistry. The second is that I should also bring in titles from my own field of expertise. In this respect, in 2003, I was coeditor of Volume 40 of the series *Analysis and Fate of Surfactants in the Aquatic Environment*, together with my two old friends, Thomas Knepper and Pim de Voogt. In 2007, and 10 volumes later, Volume 50 was published, again with me as coeditor together with my colleague Mira Petrovic. This was for the first edition of the present book *Analysis, Fate and Removal of Pharmaceuticals in the Water Cycle*. Now, in 2013, I am again coeditor of the second edition now in your hands, with a slightly modified title including the effects and risks, and we also have another colleague as coeditor, Sandra Pérez.

In the European Union, around 3000 different pharmaceutically active compounds are used in human medicine. Most modern drugs are small organic compounds, which are moderately water-soluble but still lipophilic, which allows them to be bioavailable and biologically active. They are designed to have specific pharmacological and physiological effects at low doses and thus are inherently potent, often with unintended outcomes for wildlife. Their consumption has increased over the years and will continue to increase due to the expanding population, general aging, increase of per capita consumption, expanding potential markets, and new target age groups.

After being administrated, pharmaceuticals are excreted via the liver and/or kidneys as a mixture of parent compounds and metabolites that are usually more polar and hydrophilic than the original drugs. Thus, after their usage for the intended purpose, a large fraction of these substances is discharged into wastewater, unchanged or in the form of degradation products, which are often not eliminated in conventional wastewater treatment plants. Depending on the efficiency of the treatment and chemical nature of these compounds, pharmaceuticals can reach surface and groundwaters. The need for research on the pathways of exposure, bioavailability, and risk assessment and risk management has been identified by a large number of scientists working in this field.

Pharmaceuticals commonly occur in treated sewage effluents, in surface waters, and in soil, sediments, sludge, biota, and tap water. Although the levels are generally low, there is rising concern about their potential long-term impacts on both humans and aquatic organisms, the latter being continuously

exposed to these compounds. These levels are capable of inducing acute effects in humans, that is, even though they are far below the recommended prescription dose, they have been found to affect aquatic ecosystems. Antibiotics and estrogens are among the many pharmaceuticals suspected of persisting in the environment due either to their resistance to natural biodegradation or to their continuous release.

Pharmaceuticals in the aquatic environment have been a topic of interest in conferences and in the literature for the last 20 years. One of the reasons for the increasing concern on pharmaceuticals has certainly been the improvement in analytical techniques. The use of various forms of liquid chromatography–tandem mass spectrometry includes exact mass measurement methods. It is possible to detect and confirm low levels of common pharmaceutical residues and their metabolites in water, solid, and biota samples. The fate of pharmaceuticals during sewage treatment is a key issue since wastewater treatment processes represent point source pollution of human pharmaceuticals. Investigation into removal technologies is also of high interest to the scientific community and the most common technologies being applied are included in the book. Finally, the growing occurrence of human and veterinary pharmaceuticals in the environment is driving toxicological studies and publications on ecological and risk assessment, including antibiotic resistance prioritization of the most harmful compounds with toxicity to different types of aquatic organisms, mainly daphnia, fish, and algae.

All the abovementioned topics have been included in the present book, which contains 21 chapters written by worldwide experts in the field, not only mainly from Europe and the United States but also from China. Analytical and environmental scientists will find a comprehensive view on the problems associated with the emerging and pseudopersistent problem of pharmaceutical residues in the environment. The book is addressed to a broad audience, from experts in the field to newcomers who will benefit from taking time out to familiarize themselves with its content.

Finally, I would like to thank all the authors, many of them friends and colleagues, for their efforts in compiling the literature references and writing their book chapters. I am especially thankful to my coworkers and colleagues in the department, Mira Petrovic and Sandra Pérez, for their efforts and time spent communicating with the different contributors of this comprehensive book on pharmaceuticals in the water cycle.

Damia Barcelo

Barcelona, August 2013

Preface

Pharmaceuticals are a diverse group of chemicals used in veterinary medicine, agricultural practices, human health, and cosmetic care. Many are highly bioactive, most are water soluble, and all (when present in the environment) occur usually at no more than trace concentrations.

Pharmaceuticals are a class of new, so-called “emerging” contaminants that have raised great concern in the last years. Human and veterinary drugs are continuously being released in the environment mainly as a result of the manufacturing processes, the disposal of unused or expired products, and the excreta. (i) They are referred to as “pseudo” persistent contaminants (i.e., high transformation/removal rates are compensated by their continuous introduction into environment), (ii) they are developed with the intention of exerting a desired biological effect, (iii) they often are moderately lipophilic to be able to cross membranes, and (iv) they are used by man in rather large quantities (i.e., similar to those of many pesticides).

The continuous introduction of pharmaceuticals and their bioactive metabolites into the environment may lead to a high long-term concentrations and promote continual, but unnoticed, adverse effects on aquatic and terrestrial organisms. The analytical methodology for the determination of trace pharmaceuticals in complex environmental matrices is still evolving and the number of methods described in the literature has grown considerably. Moreover, future introduction of selected pharmaceutical compounds on the regulatory lists (e.g., diclofenac) of the EU WFD and others such as carbamazepine (antiepileptic) and chloramphenicol (antibiotic) that are on the US EPA Contaminant Candidate List (CCL) as drinking water contaminants raise the interest for practical analytical methods and their applications in routine analysis. Attention has been paid during the last few years to develop a better understanding of the toxicology issues including low-dose multi-generational exposure to multiple chemical stressors and how human and ecological risks might be affected by these chemical cocktails.

The main objectives of this book is to provide the reader with a well-founded overview of the state of the art of the analytical methods for trace determination of pharmaceuticals in the environmental samples, and to give a review of the fate and occurrence of pharmaceuticals in the water cycle (elimination in wastewater and drinking water treatment), including latest developments in the treatment technologies, such as membrane bioreactors, advance oxidation, and natural attenuation processes. To reach these objectives, the book includes a concise and critical compilation of the information

published in the last years regarding the occurrence, analysis, and fate of pharmaceuticals in the environment. Following the first edition of this book in 2007, this book will extend the scope focusing on transformation products and including chapters on methods for elucidation of transformation pathways, transformation occurring in wastewater treatment processes, and transformations in the environment.

The book is structured with five parts:

The *first part* deals with the general introduction divided into two sub-chapters, the first one giving an overview of drug discovery and development in the pharmaceutical industry from the stage of compound design to clinical trials and marketing authorization. The second introduces the problem of pharmaceuticals as environmental contaminants.

The *second part* of the book is devoted to the analysis of pharmaceuticals and consists of five sub-chapters dealing with modern analytical techniques for the analysis of pharmaceuticals in the environment. It starts with discussion of needs for prioritization in selecting target compounds for chemical analysis and risk assessment. The following three chapters are devoted to highly sophisticated and established hyphenated mass spectrometric methods such as LC-MS and LC-MS-MS, and GC-MS used for target and nontarget analysis of aqueous samples (wastewater, surface, ground, and drinking water), solid matrices (soil, sediment, and sludge), and biota. In addition, sample preparation methods are thoroughly evaluated for all groups of pharmaceuticals including their major metabolites. Finally, one sub-chapter also addresses the application of bioassays and biosensors for the analysis of pharmaceuticals in the environment.

The *third part* deals with the removal of pharmaceuticals in wastewater and drinking water treatment, including also discussion of removal mechanisms. Of the treatment techniques discussed, not only conventional wastewater treatment (activated sludge) is evaluated, but also advanced treatment technologies such as biotic and abiotic membrane technologies, advanced oxidation processes, as well as natural treatments (constructed wetlands, bank filtration).

The *fourth part* gives an overview on occurrence data and fate in the aquatic and terrestrial environment, as well as an overview of evaluation of biotic and abiotic transformations in the environment through different analytical approaches.

Finally, the *fifth part* deals with the effect and risk assessment of pharmaceuticals. It will include chapters on field studies conducted to assess ecotoxicity, effects on biological communities, effects on microbial resistance, and finally evaluation on environmental risk assessment of pharmaceuticals.

The last chapter will summarize the current state of the art in the field and outline future trends and research needs.

Overall the present book is certainly timely since the interest and the developments in the analysis, fate, and removal of pharmaceuticals from the

environment have grown considerably during the last few years. This book will be of interest for a broader audience of analytical chemists and environmental scientists already working in the field of pharmaceuticals in the water cycle or newcomers who want to learn more about this emerging contamination problem.

Finally, we would like to thank all the contributing authors of this book for their time and efforts in preparing their chapters. Without their cooperation and engagement, this volume would certainly not have been possible.

Mira Petrovic, Damia Barcelo, and Sandra Pérez

Girona, July 2013

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